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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/899,922	07/09/2001	Amanda Johanne Kiliaan	BO 44633	5229

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EXAMINER	
DAVIS, RUTH A	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 02/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/899,922	KILIAAN ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2004 and 10 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment, response and affidavit filed on October 4, 2004 and December 10, 2004 have been received and entered into the case. Claims 59 – 60 are added; claims 42 – 60 are pending and have been considered on the merits. All arguments and the affidavit have been fully considered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 42 – 60 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating unipolar depression and depression related disorders, does not reasonably provide enablement for methods for preventing unipolar depressions and the claimed symptoms thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn to methods for preventing unipolar depression in persons suffering from other, named neurological disordered. Prevention provides for an expectation that a disease or disorder does not occur in response to an initiating event. While there is no requirement that prevention must be absolute in all cases, there is a reasonable expectation that some element of prevention can be shown. The standard for showing prevention or preventative effects is very

high. The standard of enablement is higher for inventions requiring prevention or preventative effects in disease conditions, since such effects may be unbelievable absent strong supporting evidence. Claims drawn to compositions with preventative effects generally require evidence because of the unpredictability in biological responses to therapeutic treatments.

Applicant has not provided convincing evidence that the claimed compositions are preventative against unipolar depression or depression related disorders. The specification is absent actual working examples of how the claimed composition exhibits preventative effects against the claimed conditions. The specification fails to teach one in the art how to administer the composition in terms of dose, duration and methodology such that one in the art could use the claimed extract to prevent the claimed diseases. For example, there is no teaching of administering the claimed composition to subjects wherein unipolar depression is prevented. The specification further fails to identify the treating population for who is at risk for such disorders and does not identify who may in included or excluded in such a population. For example, the disclosure fails to set forth if the method is intended for the general population or for someone already suffering from depression or related disorders. It would place an undue burden of experimentation on the person of ordinary skill in the art to find suitable methodologies of administering the claimed composition, such that the claimed disorders would be prevented and/or treated. Thus, the specification fails to provide sufficient guidance to allow one in the art to use the claimed invention without undue experimentation. Therefore, absent of such guidance and evidence, the specification fails to provide an enabling disclosure.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 42 – 48 and 51 – 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horrobin, Fugh-Berman, Maggioni and Growdon.

Applicant claims a method for treating and/or preventing unipolar depression or depression related disorders comprising orally administering a composition comprising (a) long chain polyunsaturated fatty acids (PUFAs) comprising omega-3 and omega-6 fatty acids in an amount of at least 350 mg/day, (b) phosphatidylethanolamine and phosphatidylcholine, and one of phosphatidylserine or phosphatidylinositol; in a ratio of 0.5 – 20; and (c) at least one compound selected from folate, vitamin B12, B6, magnesium, zinc. The composition further comprises hypericin or Withania somniera; 0.5 – 30g citrate; tryptophan or protein containing

tryptophan; one of SAMe choline, betaine or copper; one of vitamin C, E, lipoic acid, selenium salt or carotenoids; ginkgo biloba extract; or vitamin D. The omega-3 fatty acids are selected from eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and the omega-6 fatty acids are selected from arachidonic acid (ARA) and dihomogamma linolenic acid (DGLA). The (c) portion contains both folate and vitamin B6. Specifically, the composition comprises at least 120 mg long chain PUFAs, 200mg phospholipids, 200 micrograms folate, 0.1 mg hypericin or 100 mg W. somnifera, and 500 mg citrate. The phospholipids are in the amount of 1 g/day. Applicant additionally claims a method for preventing or treating unipolar depression or depression related disorders the method comprising administering a composition comprising (a) 350 mg of long chain PUFAs wherein the omega-3 fatty acids are EPA and DHA, and the omega-6 fatty acids are AA and DHGLA at a ratio of 2.5 – 5.5:1; (b) at least 2 phospholipids selected from phosphatidylethanolamine and phosphatidylcholine, and one of phosphatidylserine or phosphatidylinositol; (c) a compounds selected from folate, vitamin B12, B6, magnesium, zinc. Specifically, at least 20 mg EPA, 50 mg DHA, 50 mg AA, 200 mg phospholipids, 200 mg folate, 0.2 mg hypericin or 500 mg W.somnifera, 100 mg Mg, 5 mg Zn, 2 mg vitamin B6, 2 micrograms B12 and 1 g citrate. Applicant finally claims the method wherein the composition comprises 350 mg long chain PUFAs; at least 2 phospholipids selected from phosphatidylethanolamine, phosphatidylcholine, phosphatidylserine or phosphatidylinositol; a compound selected from folate, vitamin B12, B6, magnesium, zinc; and 4 – 40 micrograms of vitamin D3.

Horrobin teaches compositions and methods for treating depression and anxiety, the compositions comprising DHA (p.3,4), ascorbic acid (vitamin C), vitamin E, beta carotene,

selenium, zinc, and vitamin B6 (p.5,7, claims). The composition may further comprise EPA, DGLA, and AA, (p.6). Specifically, dosages of at least 350 mg DHA are combined with 250 – 2000 mg of the other named fatty acids (p.6). Examples further include vitamins of the B group, vitamin D, folic acid (folate), magnesium, and lipoic acid (examples).

Fugh-Berman teaches St. John's Wort, or hypericine (p.713), ginkgo biloba (p.715-16), vitamin B12, folate (p.721), SAMe, and tryptophan (p.722) improve depression and symptoms thereof.

Growdon teaches methods for treating depression and related disorders comprising administering lecithin (consists of phosphatidylcholine, phosphatidylethanolamine, and phosphatidylinositol, see attached "Soy Lecithin Fact Sheet") (abstract, col. 1-3).

Maggioni teaches phosphatidylserine for treating depression and symptoms thereof (abstract).

The above references do not teach a composition comprising all of the combined ingredients. However, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to combine the instant ingredients for their known benefit, as disclosed by the cited references above, since each is well known in the art for their claimed purpose. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to combine each of the claimed ingredients together with a reasonable expectation for successfully treating depression. Although the references do not teach the specific amounts or ratios as claimed, it would have been well within the purview of one of ordinary skill in the art to optimize such amounts and/or ratios as a matter of routine experimentation. In addition, although the references do not specifically teach inclusion of citrate, citrate was a well known

stabilizer and synergist with various vitamins (as admitted by applicant, specification p.5). It would have been obvious to one of ordinary skill in the art to include citrate as a matter of routine practice at the time the claimed invention was made. This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman,* 1943 C.D. 518.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

6. Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Horrobin, Growdon and Pollack.

Applicant claims a method for treating and/or preventing unipolar depression and depression related disorders comprising orally administering a composition comprising (a) long chain polyunsaturated fatty acids (PUFAs) comprising omega-3 and omega-6 fatty acids in an amount of at least 350 mg/day, (b) phosphatidylethanolamine and phosphatidylcholine, and one of phosphatidylserine or phosphatidylinositol; in a ratio of 0.5 – 20; and (c) at least one compound selected from folate, vitamin B12, B6, magnesium, zinc. The composition further comprises copper, with a ratio of zinc to copper of 5 – 12:1.

Horrobin teaches compositions and methods for treating depression and anxiety, the compositions comprising DHA (p.3,4), zinc, and vitamin B6 (p.5,7, claims). The composition may further comprise EPA, DGLA, and AA, (p.6). Specifically, dosages of at least 350 mg

DHA are combined with 250 – 2000 mg of the other named fatty acids (p.6). Examples further include vitamins of the B group, folic acid (folate), magnesium, and lipoic acid (examples).

Growdon teaches methods for treating depression and related disorders comprising administering lecithin (consists of phosphatidylcholine, phosphatidylethanolamine, and phosphatidylinositol, see attached "Soy Lecithin Fact Sheet") (abstract, col. 1-3).

Pollack teaches methods for treating depression comprising administering compositions comprising vitamin B6 (pyridoxine), copper and magnesium (abstract, claims 8-14).

The above references do not teach a composition comprising all of the combined ingredients. However, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to combine the instant ingredients for their known benefit, as disclosed by the cited references above, since each is well known in the art for their claimed purpose. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to combine each of the claimed ingredients together with a reasonable expectation for successfully treating depression. Although the references do not teach the specific amounts or ratios as claimed, it would have been well within the purview of one of ordinary skill in the art to optimize such amounts and/or ratios as a matter of routine experimentation. It would have been obvious to one of ordinary skill in the art to include citrate as a matter of routine practice at the time the claimed invention was made. This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman,* 1943 C.D. 518.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

7. Claim 50 is rejected under 35 U.S.C. 103(a) as being unpatentable over Horrobin, Growdon and Takeda.

Applicant claims a method for treating and/or preventing unipolar depression and depression related disorders comprising orally administering a composition comprising (a) long chain polyunsaturated fatty acids (PUFAs) comprising omega-3 and omega-6 fatty acids in an amount of at least 350 mg/day, (b) phosphatidylethanolamine and phosphatidylcholine, and one of phosphatidylserine or phosphatidylinositol; in a ratio of 0.5 – 20; and (c) at least one compound selected from folate, vitamin B12, B6, magnesium, zinc. The composition further comprises at least one of carnitine, B1, B5 or CoEnzyme Q10.

Horrobin teaches compositions and methods for treating depression and anxiety, the compositions comprising DHA (p.3,4), zinc, and vitamin B6 (p.5,7, claims). The composition may further comprise EPA, DGLA, and AA, (p.6). Specifically, dosages of at least 350 mg DHA are combined with 250 – 2000 mg of the other named fatty acids (p.6). Examples further include vitamins of the B group, folic acid (folate), magnesium, and lipoic acid (examples).

Growdon teaches methods for treating depression and related disorders comprising administering lecithin (consists of phosphatidylcholine, phosphatidylethanolamine, and phosphatidylinositol, see attached "Soy Lecithin Fact Sheet") (abstract, col. 1-3).

Takeda teaches compositions for treating depression comprising carnitine and vitamin B1 (abstract).

The above references do not teach a composition comprising all of the combined ingredients. However, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to combine the instant ingredients for their known benefit, as disclosed by the cited references above, since each is well known in the art for their claimed purpose. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to combine each of the claimed ingredients together with a reasonable expectation for successfully treating depression. Although the references do not teach the specific amounts or ratios as claimed, it would have been well within the purview of one of ordinary skill in the art to optimize such amounts and/or ratios as a matter of routine experimentation. It would have been obvious to one of ordinary skill in the art to include citrate as a matter of routine practice at the time the claimed invention was made. This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman,* 1943 C.D. 518.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicant argues that the references do not teach treating unipolar depression, but mood disorders; that the claimed composition has improved effects of treating depression; that citrate is an important ingredient in treating antidepression; the references do not teach vitamin D; and

that the claimed ratios are not taught by the cited references. Applicant additionally argues the references individually. Applicant provides a declaration stating that the supplemented diet is better in treating depression than a diet without the supplement.

However, these arguments fail to persuade because the claims are drawn to treating unipolar depression or depression related disorders. It is maintained that each of the references teach the various components of the claimed composition as effective for treating depression and/or depression related disorders. Specifically, anxiety and insomnia, which are defined by applicant as depression and depression related disorders (specification, p. 14).

Regarding applicant's assertion that citrate and vitamin D are not disclosed, but are important to the method of treating unipolar depression, it is noted that these limitations are not recited in the independent claims. It is further noted that applicant admits that citrate is a well known and commonly used stabilizer in pharmaceutical compositions and does not identify this component as exhibiting antidepressive qualities.

Regarding the ratios, at stated in the above rejections, it would have been well within the purview of one of ordinary skill in the art to optimize the amounts and ratios of ingredients, since were well known to have the same activity as the claimed purpose. Furthermore, it is noted that the ratios do not appear to impart unexpected advantages or results to the claimed composition.

Regarding the submitted affidavit, the compositions described in the affidavit are not the same as the claimed composition, thus is not commensurate in scope with the claimed method. In order to provide convincing evidence of an unexpected advantage or benefit, the evidence must be commensurate in scope with the claimed composition and method.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 571-272-0915. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ruth A. Davis
February 16, 2005
AU 1651

LEON B. LANKFORD, JR.
PRIMARY EXAMINER